

CLAIM REJECTIONS

Rejection of claims under 35 U.S.C. §112, first paragraph

Enablement

Claims 1, 4, 15, 17-19, 22, 30-32, 34, 39 and 50 are rejected under 35 U.S.C. §112, first paragraph. According to the Examiner “[t]he claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.” (Office Action of Sept. 25, 2003, pg. 4, para. 2). The Examiner further states that this is “a new ground of rejection necessitated by Applicants’ amendment.” (Id., pg. 2, para. 4). Applicants’ respectfully submit that the Examiner has not stated a new ground of rejection as evidenced by the Examiner’s response to the Applicants’ arguments on pages 10-12 of the Office Action. Applicants respectfully traverse this rejection with respect to the claims as amended herein.

The Applicants respectfully assert that the Examiner misapplied the test for enablement by mischaracterizing the invention and the claims. First, the Examiner seems to have focused on one aspect of the Applicant’s invention: gene therapy and/or nucleic acid immunization. In fact the Examiner appears to have mischaracterized the Applicants’ invention as having “the sole purpose of gene therapy and/or nucleic acid immunization or for obtaining therapeutic effects in general.” (Office Action, supra, page 4, first full paragraph, emphasis added). To support this statement the Examiner refers to a section of the specification that the

present invention, including coacervates and methods of using them, may deliver a recombinant virus particle containing a transgene in a controlled release manner for gene transfer applications and gene therapy. In certain embodiments, a delivery agent may be encapsulated in the coacervate to facilitate the intracellular delivery of any bioactive substance. (page 3, lines 1-5).

The Examiner, however, fails to mention that these are merely “certain embodiments” of the Applicants’ invention. (page 2, line 31). Thus, Applicants submit that it cannot be the case that the “sole purpose” of the Applicants’ invention is for gene therapy.

Many purposes of delivering nucleic acids are well-known in the art, such as producing cells in culture, in tissues or organisms that contain transgenes, deletion mutations, anti-sense

RNA's, etc. The uses of such cells include but are not limited to determining the transcriptional regulation of a gene, identifying compounds that regulate the activity of a gene product, producing high levels of a protein, determining the function of the a gene product, etc (see pages 36-42 of the specification). As these uses for a nucleic acid delivery system have been recognized for decades and are well-known in the art, the specification "need not teach, and preferably omits, what is well-known in the art." (MPEP § 2164.01, *citing*, amongst others, *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987)).

As cited in MPEP 2164.01(c),

"...when a compound or a composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for nonenablement based on how to use. If multiple uses for claimed compounds or compositions are disclosed in the application, then an enablement rejection must include an explanation, sufficiently supported by the evidence, why the specification fails to enable each disclosed use. In other words, if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention."

Thus, this section of the MPEP supports Applicants' assertion that the claims are enabled.

Similarly, the Examiner refers to another section of the specification that

[i]n another aspect, the coacervates of the present invention, and methods of using the same may be used to effect DNA vaccination, whereby the bioactive substance is a nucleic acid that expresses an antigen to provoke an immunogenic response in the host. (page 3; lines 17-19).

Here, the Examiner fails to mention the next sentences that states, "[i]n still another aspect, the coacervates of the present invention, and methods of using the same, may be used in diagnostic applications." (page 3, lines 19-21). Thus, Applicants submit that it cannot be the case that the "sole purpose" of the Applicants' invention is for nucleic acid immunization or for obtaining therapeutic effects in general.

In addition to mischaracterizing the Applicants' invention, Applicants respectfully submit that the Examiner has mischaracterized the claims. The Applicants remind the Examiner that

“[t]he enablement requirement refers to the requirement of 35 U.S.C. 112, first paragraph that the specification describe how to make and how to use the invention. The invention that one skilled in the art must be enabled to make and use is that defined by the claim(s) of the particular application or patent.” (MPEP § 2164, emphasis added).

This statement makes clear that the inquiry focuses on invention as defined by the claims. Thus, it is paramount that the claims be properly construed. In rejecting claims 1, 4, 15, 17-19 and 22, the Examiner stated that these claims were “drawn to a composition for controlled release of a nucleic acid...wherein the microsphere when administered to [an] host, provides controlled release of an expression vector.” (Office Action, page 3, first full paragraph, emphasis original). This element that the microsphere be administered to a host was only present in claim 17 and thus should not have been attributed to claims 1, 4, 15 and 22. In another portion of the Office Action, the Examiner attributes the elements of “preparing a pharmaceutical preparation” and “obtaining therapeutic effects” to claims 1, 4, 15 and 17-19. (Office Action, page 4, first full paragraph). These elements, however, are not present in claims 1, 4, 15 and 17-19. Finally, the Examiner focuses the discussion of the *In re Wands* factors starting at subsection (b) on page 5 to gene therapy, which is not present in the rejected claims.

By attributing elements to claims 1, 4, 15, 17-19 and 22 that are not present in these claims, the Examiner violated the doctrine of claim differentiation in which it is improper to read into an independent claim an element explicitly set forth in another claim. *Environmental Designs Ltd. v. Union Oil Co. of California*, 713 F.2d 693 (Fed. Cir. 1985), *cert. denied*, 464 U.S. 1043 (1984). Additionally, when a claim does not contain a certain element and another claim does, that element cannot be read into the former claim. *Tandon Corp. v. U.S. Int'l Trade Comm'n*, 831 F.2d 1017 (Fed. Cir. 1987). Therefore the Examiner cannot apply elements from one claim to all claims. Thus, the Examiner has misapplied the test of enablement to claims 1, 4, 15, 17-19 and 22. As described in the next section, the Applicants believe that these claims are fully enabled.

Furthermore, claims 17-19 have been amended to make clear that the nucleic acid is delivered to a “target cell,” which is defined as being *in vitro*, *in vivo* or *ex vivo* cells that have been provided with a specified vector. (page 10, lines 14-17). As described above, such uses of target cells have been recognized for decades and are well-known in the art. (MPEP § 2164.01,

citing, amongst others, *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987)). In addition, the Applicants have taught a new way of making such target cells. The Applicants submit that they have fully enabled compositions for controlled release of a nucleic acid in a target cell as set forth in claims 1, 4, 15, 17-19 and 22.

Applicants have also amended claim 30 to make clear that the nucleic acid be delivered to a “target cell.” As uses of such cells are well-known in the art and the Applicants’ teaching of how to make such target cells, the Applicants have fully enabled compositions for controlled release of a nucleic acid in a target cell as set forth in claim 30.

Regarding the rejection of claim 50, the Examiner seems to have confused the role of viruses in causing cancer and viruses that can be used to deliver a nucleic acid to a cell. The Applicants have shown that a virus can be used to deliver a reporter gene (luciferase) to the cancer cell. For decades practitioners have used reporter genes to measure the successful incorporation and expression of nucleic acids in target cells.

To support this, Applicants submits for the Examiner’s consideration U.S. Patent No. 6,008,202 entitled “Stable lipid-comprising drug delivery complexes and methods for their production” by Huang et al. (cited in the accompanying IDS). U.S. Patent No. 6,008,202 has claims drawn to “Novel stable, concentrated, biologically active and ready-to-use lipid-comprising drug delivery complexes and methods for their production are described. The biological activity of the complexes produced are comparable to the formulations prepared according to the prior art admixture method and upon purification, the complexes produced by the method of this invention are 50 to 500 fold more concentrated than the complexes formed by admixture.” (Abstract). Applicants further direct the Examiner to Example 17 where Huang et al. used lipid-comprising drug delivery complexes to transfect and express “pRSVL, a plasmid which encodes the luciferase gene” to inject nude mice that were inoculated intraperitoneally with SKOV-3 human ovarian carcinoma cells. Tumor nodules from such mice were subsequently examined and found to express luciferase. In this patent, Huang et al. discloses working examples that utilize luciferase or CAT reporter genes. Applicants respectfully point out that the Abstract of this patent states that “[t]he method described herein provides for the

large scale production of lipid-comprising drug delivery systems useful for gene therapy and other applications”.

Thus, Applicants submit that one skilled in the art would recognize that successful expression of a reporter gene reasonably predicts the incorporation and expression of other genes. As the Applicants have taught how to make and use the invention in claim 50, Applicants submit that they have fully enabled the scope of this claim.

Applicants respectfully request reconsideration and withdrawal of all rejections under 35 U.S.C. §112, second paragraph, insofar these may apply to the amended claims.

Rejection of claims under 35 U.S.C. §112, second paragraph

The Examiner has rejected claims 24-26, 28 and 45 under 35 U.S.C. §112, second paragraph allegedly “as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.” Applicants respectfully traverse this rejection.

Specifically, the Examiner has pointed out that “[c]laim 24 and its dependent claims recite the limitation “said a viral vector” in line 2 of claim 24” and that “[t]here is insufficient antecedent basis for this limitation in the claim” as “[t]here is no recitation of any viral vector in claim 1 on which claim 24 is dependent.” In order to expedite prosecution and not in acquiescence to the rejections, Applicants have amended claim 24 to recite “wherein said delivery agent is a virus, a viral particle or a viral vector”. With respect to this amendment, Applicants believe that claim 24 and its dependent claims 25 and 26 are fully in accord with the support provided with the specification and that the amendment provides metes and bounds to the claim.

Claim 45 has been rejected “as being incomplete for omitting essential steps, such omission amounting to a gap between the steps” wherein “[t]he omitted step is the step of preparing the microspheres for administration to a host”. The Examiner has further rejected claim 50 for having “insufficient antecedent basis for the limitation “the target site” in the claim.

The Examiner's helpful comments have been considered and Applicants believe that the amendments made herein fully overcome and obviate the stated grounds for rejection of said claims.

Applicants respectfully request reconsideration and withdrawal of all rejections under 35 U.S.C. §112, second paragraph, insofar these may apply to the amended claims.

Rejection of claims under 35 U.S.C. §102(e) over Russell-Jones et al.

The Examiner has rejected claims 1, 10-12 and 29 under 35 U.S.C. §102(e) as allegedly being anticipated by Russell-Jones et al (U.S. Patent No. 6,159,502). The Examiner further states that this is "a new ground of rejection". Applicants respectfully traverse this rejection. In order to anticipate a claim, each and every element of the claim must be found in a single prior art reference.

Claim 1 as amended and dependent claims thereon, are drawn to a composition for controlled release of a nucleic acid comprising a coacervate microsphere crosslinked by a crosslinking agent comprising a metal cation; a nucleic acid incorporated in said coacervate microsphere; and a delivery agent incorporated in said coacervate microsphere, wherein the coacervate microsphere comprises a polycationic and a polyanionic molecule other than said nucleic acid and the delivery agent is other than said poly cationic molecule of the coacervate microsphere. Claim 29 as amended, is drawn to a gene delivery system for transducing cells, comprising: a coacervate microsphere crosslinked by a crosslinking agent comprising a metal cation that encapsulates at least a nucleic acid and a delivery agent that is other than a polycation of the coacervate microsphere, for facilitating intracellular delivery of said nucleic acid, wherein upon contact of cells with said coacervate microsphere, controlled release of said nucleic acid results in transduction of the cells by said nucleic acid.

The Examiner relies on Russell-Jones et al. as teaching,

"the preparation for complexes and compositions for oral delivery of a substance or substances to the circulation or lymphatic drainage system of a host. The complexes comprise a microparticle or microsphere coupled to at least one carrier (e.g., mucosal binding proteins, bacterial adhesions, viral adhesions, lectins, Vitamin B12), the carrier

being capable of enabling the complex to be transported to the circulation or lymphatic drainage system via the mucosal epithelium of the host, and the microparticle, or microsphere being capable of encapsulating the substances.”

Russell-Jones et al. does not disclose “a coacervate microsphere crosslinked by a crosslinking agent comprising a metal cation”. Because Russell-Jones et al. does not disclose each and every element of the claims, the Applicants respectfully submit that this reference does not anticipate claims 1, 10-12 and 29. Accordingly, Applicants respectfully request the withdrawal of the rejection of claims 1, 10-12 and 29 under 35 U.S.C. §102(e).

Rejection of claims under 35 U.S.C. §102(b) over Spence et al.

The Examiner has rejected claims 1, 7, 11, 29, 40 and 42-45 under 35 U.S.C. §102(b) as allegedly being anticipated by Spence et al. (U.S. Patent No. 4,325,937). The Examiner further states that this is “a new ground of rejection”. Applicants respectfully traverse this rejection.

Claim 7 has been cancelled rendering the instant rejection moot with respect to this claim.

Claim 1 as amended and dependent claims thereon, is drawn to a composition for controlled release of a nucleic acid comprising a coacervate microsphere crosslinked by a crosslinking agent comprising a metal cation; a nucleic acid incorporated in said coacervate microsphere; and a delivery agent incorporated in said coacervate microsphere, wherein the coacervate microsphere comprises a polycationic and a polyanionic molecule other than said nucleic acid and the delivery agent is other than said poly cationic molecule of the coacervate microsphere.

Claim 29 as amended, is drawn to a gene delivery system for transducing cells, comprising: a coacervate microsphere crosslinked by a crosslinking agent comprising a metal cation that encapsulates at least a nucleic acid and a delivery agent that is other than a polycation of the coacervate microsphere, for facilitating intracellular delivery of said nucleic acid, wherein upon contact of cells with said coacervate microsphere, controlled release of said nucleic acid results in transduction of the cells by said nucleic acid.

Claim 40 as amended and dependent claims thereon, is drawn to a method for preparing a gene delivery system, comprising preparing a first solution of polycationic molecules and a second solution of polyanionic molecules; adding to either said first solution or said second solution a nucleic acid; and adding to either said first solution or said second solution a delivery agent; combining said first solution and said second solution to form a third solution comprising the nucleic acid and the delivery agent; and, isolating coacervate microspheres formed from a portion of said polycationic molecules and a portion of said polyanionic molecules from said third solution and treating said coacervate microsphere with metal cations, wherein said coacervate microspheres encapsulate at least a portion of said nucleic acid and said delivery agent and said coacervate microspheres are crosslinked by a crosslinking agent comprising a metal cation.

The Examiner relies on Spence et al. as teaching a

“microbial composition comprising: (a) a microbial insect pathogen of viral (e.g. Douglas fir tussock moth NPV viruses, Autographa californica NPV viruses, T-4 bacterial phages), bacterial, or fungal origin (b) a coacervate microbead in spherical form which is comprised of a nucleic acid, typically RNA, and a proteinaceous material (e.g., gelatin, protamine, cytochrome c), whereby the microbead structure itself effectively shields the pathogen from sunlight-induced activation and that the microbead is typically stabilized by chemical crosslinking...Spence et al. teach also a method for preparing the same composition, comprising: (a) preparing an aqueous solution containing a nucleic acid (a polyanion); (b) preparing an aqueous solution containing a proteinaceous material; (c) preparing an aqueous suspension of strongly positive or negatively surface-charged microbial insect pathogens; and (d) mixing the aqueous solutions and suspension prepared in steps (a), (b), and (c) together, thereby spontaneously forming microbeads having the insect pathogens embedded therein, or in a preferred embodiment the suspension prepared in step (c) is first mixed with the solution prepared in step (a) and then this mixture is mixed with the solution prepared in step (b), or in a preferred embodiment the suspension prepared in step (c) is first mixed with the solution prepared in step (b) and then this mixture is mixed with the solution prepared in step (a)...”

As stated previously, a claim is anticipated only if each and every element of the claim is found in a single prior art reference. Spence et al. does not disclose “a coacervate microsphere crosslinked by a crosslinking agent comprising a metal cation”. Because Spence et al. does not disclose each and every element of the claims, the Applicants respectfully submit that this reference does not anticipate claims 1, 7, 11, 29, 40 and 42-45. Accordingly, Applicants respectfully request the withdrawal of the rejection of claims 1, 7, 11, 29, 40 and 42-45 under 35 U.S.C. §102(b).

Rejection of claims under 35 U.S.C. §103

Claims 1, 4-6, 13-19, 23-26, 28, 30-31, 33-39 and 48 are rejected under 35 U.S.C. §103 (a) as allegedly being unpatentable over Russell-Jones et al. (U.S. Patent No. 6,159,502) in view of Beer et al. (Adv. Drug Delivery Reviews 27:59-66, 1997). The Examiner further states that this is “a new ground of rejection necessitated by Applicants’ amendment.” Applicants’ respectfully submit that the Examiner has not stated a new ground of rejection as evidenced by the Examiner’s response to the Applicants’ arguments on pages 20-22 of the Office Action. Applicants respectfully traverse this rejection.

In order to render a claimed invention obvious, the combined teachings of prior art references must disclose or suggest **all** elements of the invention, or motivate a person skilled in the art to modify the reference teachings so as to arrive at the claimed invention.

Russell-Jones et al. (US 6,159,502) describes a microparticle or microsphere system for oral delivery of substances which would otherwise be degraded within the gastrointestinal tract. Specifically, the Russell-Jones microparticles rely on the use of a carrier defined as “including mucosal binding proteins, Vitamin B12, and analogues or derivatives of Vitamin B12 possessing binding activity to Castle’s intrinsic factor” (col. 4, lines 34-37). Beer et al. (1997), 27 Advanced Drug Delivery Reviews 59-66, report the results of preliminary experiments on the microencapsulation of recombinant adenovirus using PGLA (poly lactic-glycolic acid) (page 63, col. 2, lines 10-12, and page 61, col. 1, line 17 to col. 2, line 9).

Claims 1, 30, 35, 36, 38, 39, 48 as amended and dependent claims thereon, recite “coacervate microspheres crosslinked by a crosslinking agent comprising a metal cation”. Applicants urge that the combined teachings of Russell-Jones et al. (U.S. Patent No. 6,159,502) or Beer et al. (Adv. Drug Delivery Reviews 27:59-66, 1997) are devoid of any teaching, suggestion, motivation, or guidance for “coacervate microspheres crosslinked by a crosslinking agent comprising a metal cation”. Applicants respectfully submit that the claimed invention cannot be deemed obvious in light of the combined teachings of these two references.

Applicants respectfully request the withdrawal of the rejection of claims 1, 4-6, 13-19, 23-26, 28, 30-31, 33-39 and 48 under 35 U.S.C. §103 (a).

Claims 1, 7, 21, 40 and 42-47 are rejected under 35 U.S.C. §103 (a) as being unpatentable over Russell-Jones et al. (U.S. Patent No. 6,159,502) in view of Beer et al. (Adv. Drug Delivery Reviews 27:59-66, 1997) and Leong et al. (U.S. Patent No. 5,759,582). The Examiner further states that this is “a new ground of rejection”.

Applicants respectfully traverse this rejection.

Claim 7 has been cancelled rendering the instant rejection moot with respect to this claim.

Claim 1 as amended and dependent claims thereon, is drawn to a composition for controlled release of a nucleic acid comprising a coacervate microsphere crosslinked by a crosslinking agent comprising a metal cation; a nucleic acid incorporated in said coacervate microsphere; and a delivery agent incorporated in said coacervate microsphere, wherein the coacervate microsphere comprises a polycationic and a polyanionic molecule other than said nucleic acid and the delivery agent is other than said poly cationic molecule of the coacervate microsphere.

Claim 40 as amended and dependent claims thereon, is drawn to a method for preparing a gene delivery system, comprising preparing a first solution of polycationic molecules and a second solution of polyanionic molecules; adding to either said first solution or said second solution a nucleic acid; and adding to either said first solution or said second solution a delivery agent; combining said first solution and said second solution to form a third solution comprising the nucleic acid and the delivery agent; and isolating coacervate microspheres formed from a portion of said polycationic molecules and a portion of said polyanionic molecules from said third solution and treating said coacervate microsphere with a metal cation, wherein said coacervate microspheres encapsulate at least a portion of said nucleic acid and said delivery agent and said coacervate microspheres are crosslinked by a crosslinking agent comprising a metal cation.

Claim 47 as amended is drawn to a coacervate microsphere for transfection and expression of a recombinant protein prepared by the process comprising in any order: adding a polycationic molecule to a first aqueous solution; adding a polyanionic molecule to a second aqueous solution; and, adding to either said first or said second solution a virus comprising a viral vector comprising a nucleic acid encoding a recombinant protein and at least one regulatory element; mixing said first and second solution together to form a coacervate microsphere of said polycationic molecule and said polyanionic molecule encapsulating said virus; and, isolating said coacervate microsphere and treating said coacervate microsphere with a metal cation, wherein said coacervate microsphere is crosslinked by a crosslinking agent comprising a metal cation and releases said virus in vivo or in vitro, whereby said virus transfects cells, resulting in expression of said recombinant protein.

Leong et al. (U.S. 5,759,582) describe the preparation of coacervate microspheres and their use to encapsulate pharmaceutically active substances (col. 4, lines 48-67). The Leong reference does not disclose “a coacervate microsphere crosslinked by a crosslinking agent comprising a metal cation”. Accordingly, the Leong reference does not provide any incentive, motivation, or guidance for overcoming the Russell-Jones and Beer omission of “a coacervate microsphere crosslinked by a crosslinking agent comprising a metal cation.” The Leong et al. reference thus fails to remedy the defects noted above with respect to the Russell-Jones and Beer combination. This rejection of claims 1, 7, 21, 40 and 42-47 under 35 U.S.C. §103 (a) is insufficient to render the instant invention obvious. Applicants respectfully submit that this rejection be reconsidered and withdrawn.

Claims 1, 4-6, 13-19, 22, 30 and 49 remain rejected under 35 U.S.C. §103 (a) as being unpatentable over Russell-Jones et al. (U.S. Patent No. 6,159,502) in view of McElligott et al. (WO 94/23738). The Examiner further states that this is “a new ground of rejection.” Applicants’ respectfully submit that the Examiner has not stated a new ground of rejection as evidenced by the Examiner’s response to the Applicants’ arguments on pages 26-27 of the Office Action. Applicants respectfully traverse this rejection.

Claim 1 as amended and dependent claims thereon, is drawn to a composition for controlled release of a nucleic acid comprising a coacervate microsphere crosslinked by a

crosslinking agent comprising a metal cation; a nucleic acid incorporated in said coacervate microsphere; and a delivery agent incorporated in said coacervate microsphere, wherein the coacervate microsphere comprises a polycationic and a polyanionic molecule other than said nucleic acid and the delivery agent is other than said poly cationic molecule of the coacervate microsphere.

Claim 30 as amended, is drawn to a method for delivering a nucleic acid into a cell, comprising: contacting a cell with a composition comprising a coacervate microsphere crosslinked by a crosslinking agent comprising a metal cation, wherein: said coacervate microsphere incorporates a nucleic acid contained in a transfer vector having at least one regulatory element; said coacervate microsphere comprises a polycationic molecule and a polyanionic molecule other than said nucleic acid; and said coacervate microsphere incorporates a delivery agent, wherein said contacting of a cell with said composition results in controlled release of said transfer vector in the cell.

McElligott et al. (WO 94/23738) teaches the microencapsulation of nucleic acids, wherein the nucleic acid is conjugated chemically to a promoting material that promotes uptake into cells, transport to the cell nucleus, or expression of nucleic acid in the cell. The McElligott reference does not provide any incentive, motivation, or guidance for using or making coacervate microsphere crosslinked by a crosslinking agent comprising a metal cation. As such, the combined teachings of Russell-Jones et al. (U.S. Patent No. 6,159,502) and McElligott et al. (WO 94/23738) do not render the instant invention obvious with respect to claims 1, 4-6, 13-19, 22, 30 and 49. Applicants respectfully submit that this rejection be reconsidered and withdrawn.

Thus, Applicants respectfully request reconsideration and withdrawal of these rejections under 35 U.S.C. §103(a).

CONCLUSION

Applicants have, by way of the amendments and remarks made herein, obviated or rendered moot each of the rejections set forth in the September 25, 2003 Office Action. Applicants respectfully urge that the amended application is in condition for allowance. Favorable reconsideration and early allowance thereof are respectfully solicited.

If the Examiner has any questions, or believes that a teleconference would facilitate the further prosecution of this application, the Examiner is urged to contact the undersigned at the telephone number listed below.

Customer No. 25181
155 Seaport Boulevard
Boston, MA 02210
Tel: (617) 832-1000
Fax: (617) 832-7000
Date: February 25, 2004

Respectfully submitted,
Foley, Hoag LLP
By: 
Lauren T. Knapp
Reg. No. 45,605
Attorney for Applicants